**DOCKET NO.:** ISIS-5320 **Application No.:** To be assigned

Preliminary Amendment - First Action Not Yet Received

## Amendments to the Specification:

Please amend the title as follows:

--IMPROVED PROCESS PROCESSES FOR THE SYNTHESIS OF 2'-O-SUBSTITUTED PYRIMIDINES AND OLIGOMERIC COMPOUNDS THEREFROM--.

Please amend the paragraph at page 1, lines 1-9 of the specification as follows:

## -- CROSS REFERENCE TO RELATED APPLICATIONS

This application is a divisional application of United States application serial number 09/747,009, filed December 22, 2000, which is a continuation of United States application serial number 08/894,899, filed January 7, 1998, now issued as United States Patent number 6,222,025, which is the National Stage of International Patent Application PCT/US96/03174, filed March 6, 1996 and a continuation-in-part of United States application serial number 08/475,467, filed June 7, 1995, now issued as United States Patent number 5,760,202, also identified by attorney docket number ISIS-1965 which is a continuation-in-part of United States application serial number 08/398,901, filed March 6, 1995, now issued as United States Patent number 6,166,197 also identified by attorney docket number ISIS-0719. The contents of the foregoing patent applications are incorporated herein by reference.--

Please amend Table 1 on page 60, lines 1-16 of the specification as follows:

Table 1
Modified oligoribonucleotide sequences used in nuclease studies

2'-O-substitution	backbone	17-mer	12-mer
2'-deoxy	P=O	SEQ ID NO:1	SEQ ID NO:6
methyl	P=O	SEQ ID NO:2	SEQ ID NO:7
propyl	P=O	SEQ ID NO:3	SEQ ID NO:8
pentyl	P=O	SEQ ID NO:4	SEQ ID NO:9
2'-deoxy	P=S	SEQ ID NO:5	SEQ ID NO:10

17-mer: 2'-deoxy (P=O)

5' GGA CCG GAA GGTACGA 3' (SEQ ID NO:1)

methyl

5' GGA CCG GAA GGU ACG AG 3' (SEQ ID NO:2)

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propyl		5' GGA CCG GAA GGU ACG AG 3'	(SEQ ID NO:3)
pentyl		5' GGA CCG GAA GGU ACG AG 3'	(SEQ ID NO:4)
2'-deoxy	(P=S)	5' GGA CCG GAA GGT ACG AG 3'	(SEQ ID NO:5)
12-mer:all		5' CUA AGC AUG UCA 3'	(SEQ ID NO:6)

underlined = 2'-modified residues

Please amend the paragraph spanning page 64, lines 26 to page 65, line 13 as follows:

Sequences s	tudied:	
SEQ ID NO:	15-mers	sequence
12	2'-deoxy	<u>CoGoAoCoToAoToGoCoAoAoGoToAoC</u>
13	methy methyl	CoGoAoCoToAoToGoCoAoAoGoToAoC
14	propyl	CoGoAoCoToAoToGoCoAoAoGoToAoC
15	pentyl	<u>CoGoAoCoToAoToGoCoAoAoGoToA</u> oC
16	RNA	CoGoAoCoToAoToGoCoAoAoGoToAoC
	17-mers	
17	2'-deoxy	<u>GoGoAoCoCoGoGoAoAoGoGoToAoCoGoAoG</u>
18	methy methyl	GoGoAoCoCoGoGoAoAoGoGoUoAoCoGoAoG
19	propyl	GoGoAoCoCoGoGoAoAoGoGoUoAoCoGoAoG
20	pentyl	GoGoAoCoCoGoGoAoAoGoGoUoAoCoGoAoG
21	RNA	GoGoAoCoCoGoGoAoAoGoGoToAoCoGoAoG
	18-mers	
22	2'-deoxy	<u>TsGsGsGsAsGsCsCsAsTsAsGsCsGsAsGsG</u> sC
23	methy methyl	<u>TsGsGsGsAsGsCsCsAsTsAsGsCsGsAsGsG</u> sC
24	propyl	<u>TsGsGsGsAsGsCsCsAsTsAsGsCsGsAsGsG</u> sC
25	pentyl	<u>TsGsGsGsAsGsCsCsAsTsAsGsCsGsAsGsG</u> sC
26	RNA	TsGsGsGsAsGsCsCsAsTsAsGsCsGsAsGsGsC

underlined = 2' modified residue; o = phosphodiester linkage; s = phosphorothioate linkage-

Please amend the paragraph at page 72, lines 9-16 of the specification as follows:

--For the construction of the pSG5-rev plasmid, which expresses rev protein both in mammalian cells of *in vitro* with T7 RNA polymerase, an EcoRI/BgIII rev cDNA was prepared by PCR from pCV1. The PCR fragment was cut with EcoRI and BgIII and subcloned into the Eco/RI/BgIII sites of the vector pSG5 (Stratagene). The PCR primers were:

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5'-GCT CGG GAA TTC ATG GCA GGA AGA AGC GGA(SEQ ID NO:30)
5'-CTG GGA GAT CTC TAT TCT TTA GCT CCT GAC TC(SEQ ID NO:31).--

Please delete the Sequence Listing at pages 76-81 of the specification.